

Which came first- the biological cell or the cell membrane?

Mel Rosenberg June 3/74

INTRODUCTION

Membranes are a ubiquitous phenomenon in biological systems.¹ Every living cell has a surrounding plasma membrane which constitutes a separate ^{Compartment!} phase.² Eucaryotic cells have intracellular membranes which surround many organelles and, in some cases, themselves constitute organelles³.

The two major molecular components of biological membranes are ^{invariably} lipids and proteins. A great diversity exists, however, in the ratios of these components, in the minor components, and in the specific molecular composition.⁴

Each biological membrane is unique in composition and many have specific functions, but many similarities, not only in gross chemical composition, but also in physical and chemical behaviour⁵, molecular structure (as observed, for example in the electron microscope⁶⁻⁸) and basic biological properties⁹. These similarities have prompted the construction of a cornucopia of general membrane models^{10,11,12} and reviews thereon¹³⁻¹⁵ which attempt to reconcile similar membrane characteristics in terms of a general molecular structure.^{* See comment}

Cell membranes are essential components of the living cell, as we know it today. It is this barrier, only a few molecules in thickness, which sequesters the living metabolizing cytoplasm from the external environment. When the membrane of an erythrocyte is disrupted, the cell matter spills out into the aqueous surroundings¹⁶. Even cells which are

1. -All cells---

* The possibility is open (18---).

surrounded by thick polymeric cell walls also lose their viability unless their cell membrane is intact. Compartmentation is only one of many varied and elegant functions which can be ascribed to membranes, yet clearly illustrates their vital role in the living process.

The evolution of the biological membrane as a function of the history of life itself is a subject of speculative interest.⁵¹ Do the present similarities in biological membranes reflect a common precursor? If so, when did this membrane develop? Alternatively, do the dissimilarities in membranes indicate that they evolved under different circumstances, and perhaps in different eras? In this case, the similarities can be ascribed to parallel results in the evolutionary search of the best system to fulfil common needs. Were cells once extant which did not have a separate phase boundary?

Who came first - the biological cell or the biomembrane?

Although any conclusions on this question ~~xxx~~ would of course be impossible to verify, the teleological ~~x~~ implications are worth considering. Many scientists engaged in biological research tend to consider cell organelles in general, the membrane among them, in terms of their ^{present} functions.²⁰¹⁷ If, indeed, the membrane evolved in cells already viable and functioning, perhaps the membrane can ~~xxx~~ be thought of as an organelle whose structure arose in response to functional needs which still exist (therefore, so does the membrane). On the other

17 - Quate Lehninger

hand, recent experiments, mostly in the research of artificial membranes, lend credence to the theory first advanced by Goldacre¹⁸, which postulates that membranes of a more primitive but similar form, existed before life did, and actually provided ~~xxx~~^{the} morphological basis for the development of the cell~~x~~. If this is the case, then the similarity of biological membranes is no great wonder - they were there before ~~xxx~~ cell metabolism, genes, and biological evolution existed. If some primitive membrane was a motive force in biogenesis itself, then perhaps cell ~~funx~~ function can be appreciated in terms of membrane structure, as well as the reverse. ^{vice-versa}

Virus is a living form, since it is able to reproduct it self, but it has no membranes. Thus, life could exist without membranes. On the other hand, virus is not able to reproduce it self, unless it is embedded in a living cell surrounded by a membrane. Thus, even the most primitive life form we know, the virus, needs a membrane surrounded enviroment for its reproduction and survival. Thus, life could not exist without membranes.

REDEFINITION OF THE CELL

It would be advantageous to be able to define the cell membrane and the cell without using one for the other's definition. However, most definitions use the membrane to ~~characterize the cell~~. While the membrane may be defined as separating two aqueous phases²², the cell is much harder to define without ^{using} the membrane which surrounds it.²³ This leads us to the following ^{word} ~~semantic~~ problem: if one of the conditions for a cell is ^{the presence of} a membrane, the cell could not have preceded the membrane. We must therefore extend ~~out~~ the definition of the cell to ~~thxxxx~~ include those bodies which may have existed at one time, which were capable of the same or similar metabolic and reproductive properties as the most primitive cells we recognize today, but were either devoid of a ~~xxxx~~ separate phase membrane, or possessed a membrane of ~~xxxx~~ structure and composition removed from the biomembrane we recognize today. As well, since we are interested in the origin of the membranes we find today in living ~~xx~~ organisms, we must further that these primitive cells, also referred to as "protobionts"²⁴ or "protocells", evolved into ~~xxxx~~ living systems whose ancestors are present to this day.

The word "cytosol" is quite good for the definition

22. you are looking for. It is the cell content, without
23. its membranes and organelles.
Please reduce this page to several lines.

BASIC THEORIES OF ~~Bio~~^{CHEMICAL} EVOLUTION

A number of theories exist concerning the evolution of living systems from inorganic beginnings. The most plausible hypothesis involves the synthesis of organic molecules in a reducing atmosphere, their dissolution into the primeval oceans, followed by subsequent polymerization and organization culminating in ^a separate primitive biological system, without genes but with a basic metabolism and the ability to reproduce, and grow.

At first ^{sight} ~~site~~, the most difficult part to visualize is the separation of part of this primeval ocean into a separate physical system, in other words morphogenesis of the cell. However, at least ^{relevant} three types of systems have been investigated. The first two, ^{24,28} ~~coacervates~~ ^{protenoid} and ²⁵ ~~microspheres~~, ~~xxx~~ are microscopic drops of polymers which form spontaneously in aqueous solution. They are capable of dividing, of absorbing additional material against a concentration gradient, and of certain enzymatic ^{catalytic?} reactions, providing that the enzyme is one of the polymers present. Brief explanation of the structure of each type is needed. ←

These systems are very enlightening and show relatively simple examples of aqueous ~~xx~~ solutions in which organic and biological molecules can separate out into a separate phase with distinct morphological characteristics. What neither system does exhibit, however, is a membrane of separate phase and composition. In the coacervates, the interface with ~~xxx~~ the aqueous medium is capable of selective permeability. The proteinoid microspheres also show osmotic properties, and in the electron microscope, exhibit a membrane ²⁹. They do not however, contain any lipid, nor do they incorporate lipids. Both models are thus ~~xxxxxx~~ lacking a

what, exactly, the meaning of "osmotic properties" of the proteinoid

biological membrane, or a reasonable facsimile thereof. In addition, it is hard to reconcile present-day cells with these drops of gelled polymers. For one thing, cytoplasm is water-soluble.

THE MEMBRANE IN CHEMICAL EVOLUTION

Since the bulk of Oparin and Fox's work with the aforementioned systems, the ubiquity of the cell membrane has been recognized. ¹ in living cells

It would seem that spontaneous systems involving membranes similar to biological ones should be more credible.

^{such}
The experimental basis for artificial membrane systems in water is firmly established, using both molecules ~~xxxxxxx~~ extracted from biological membranes (such as mixtures of phospholipids ²⁹)

~~xxxxxxx~~, simpler molecules (such as long-chain alcohols and fatty-acids ³⁰) whose synthesis under primitive conditions is plausible ³¹, and combinations of lipids and specific ^{membrane} proteins ³².

These molecules are all of an amphipathic nature (they contain both polar and non-polar groups). Upon addition to water or saline solution, these ^{immiscible} molecules form layers on the top of the liquid, but upon mechanical shaking disappear into solution. Microscopic examination reveals that the molecules form low-energy aggregates among which ~~xxxxx~~ vesicles are found, consisting of a ^{thin} membrane enclosing a volume of solution. ³² Isolated cell membranes show similar behaviour. ³³

Many similarities in structure and physical properties exist between ~~xxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxx~~ biological membranes and artificial ones created with a variety of amphipathic molecules. ³⁴

~~Goldsacre~~ ³² postulated that

31 34 ~~39~~ catalyst 35.

three

rin, and Fox, and others, the membrane does not
in morphological development "protobionts" or "proto cells"
ole. Their primitive cells have a primitive com-
primitive metabolism, selective absorption. They ^{reproduce}

well without a membrane, why did they later employ one? Why can we not find today any example of a cell, however primitive, without a protein-lipid ^{basal} membrane?

DISCUSSION

The membrane hypothesis raises a number of questions. Provided that primitive membrane vesicles were around long before the development of the genetic apparatus, what connection can there be between primitive membranes, composed of a heterogeneous array of amphipathic molecules, and present biological membranes? Today, most cells synthesize their own major membranal components. These molecules are specific, and they are incorporated in controlled ratios into the membrane. * Could the primitive gene have any way of knowing what kind of membrane was surrounding him, and ~~xxx~~ code the synthesis of exactly the same molecule? Probably not. On the other hand, the gene may have coded similar molecules, which were initially incorporated into a membrane of exogeneous origin, and over a number of generations slowly phased out the non-genetic membrane components. In this case, a ^{structural} resemblance would have to exist, to enable the incorporation of genetically coded membrane molecules into a heterogeneous membrane. The ~~xxxxxx~~ basic structure would also not have been radically altered.

Support for this hypothesis comes from the Mycoplasma group of organisms, which are adept at performing the opposite phenomenon. They can incorporate a variety of extraneous fatty acids directly from the medium into their membranes.³⁶ Thus the membrane composition can be radically altered, without affecting its structure, or the viability of the microorganism.

* On the other hand, in "primitive" cells, such as mycoplasma, the composition of the membrane is changed in a wide range according to the available fatty acids in the medium.

If the earliest cells developed within a membrane, then it is likely that although they acquired the capacity for incorporating molecules into the membrane, they did not have to learn to create membranes, the membranes being present. Indeed, no organism is known today which synthesizes membranes de novo. If the membrane was the result of an evolutionary search for a particular system, then we should see the ~~existence~~ ^{capacity} today.

What happened to this genetic capacity? It can be argued that it is masked but still exists. If we were to remove a cell membrane, the cell would be able to synthesize a new one, were it not dependent ~~on~~ on the previous one to live. Alternately, the inability to synthesize ~~new~~ membranes can be ascribed to loss of a genetic capacity³⁷, in view of the fact that once the cell membrane was synthesized, the need for de novo synthesis dissipated. This, however, is not true. Eucaryotic cells have various needs for ~~intracellular~~ intracellular membranes for further compartmentation. When the need for ~~an~~ a new enclosed intracellular vesicle arises, for example, in the secretion of a hormone, ^{and other secretory proteins} no new membranes are created. The organelles are released in their membrane-bound form from the Golgi apparatus, itself a folded membrane structure.^{38, 39} Why must the eucaryotic cell have adopted such an intricate system for membrane synthesis if it is capable of de novo synthesis?

There is also evidence for direct incorporation of components which already exist in the plasma membrane.⁴⁸
One possible answer is that the loss of genetic capacity occurred during the evolution of the procaryot. While some procaryotic cells do have organelles bounded by membranes, ^(gas vacuoles) they were found to be devoid of lipids, indicating a dif-

ferent type of membrane, composed almost exclusively of protein ⁴⁰
inability of

The lack of de novo synthesis, is not, however, exclusive to membranes. Bacteria are incapable of de novo synthesis of cell wall. Genes, RNA and protein must be synthesized from their respective ~~xxx~~ templates. On the other hand, flagellae can be assembled de novo. A bacteria with a single polar flagellum divides, giving rise to two progeny, one of which must then synthesize a new polar flagellum, where none previously existed. *Why then, not membranes.*

The circumstantial evidence of what we observe in present biological systems indicates that although the membrane is vital, the genetic control over it is limited. It is true that in the normal case specific membrane proteins are coded for, and specific enzyme pathways synthesize the lipids which are incorporated in a more-or-less regulated manner ^{41, 38, 39} into a particular membrane. On the other hand, some ^{can} leeway exists in the composition of the membrane, at least in the lipid phase. In addition, cells encounter problems in synthesizing new membranes with a lipid composition. These ~~two~~ observations strengthen the hypothesis that the membrane existed in the primitive cell before the genetic apparatus developed, and in the present state of biological systems the membrane still has a modicum of the independence ~~of~~ from cellular control it once possibly had in the primeval sea.

If we further examine this point, we come to the conclusion

that perhaps the general structure and makeup of the membrane as it exists today, is ~~x~~ not the optimal one, but rather one the cell cannot rid itself of. Certainly, a great variety of thin membranes with properties of semi-permeability exist⁴³. The cell cannot, however, undergo the transition, because to disrupt the existing physical membrane continuum would cause death. *So the genetic apparatus has compensated the* ~~In addition, the~~ *inaptitudes of a random membrane of random proteins & lipids* ~~genetic control of the membrane which had and does exist~~ has adapted the membrane to acquire functions which a non-specific lipid-protein membrane would not possess intrinsically⁴⁴, such as amino-acid transport⁴⁵ and energy conversion⁴⁶. (33).

Membrane structure and cell function and metabolism seem to fit like a hand does in a glove. The question which should be asked in this case is, "Has the hand changed to fit the glove?"

Membranes are almost always considered in terms of their functional ability. The biological membrane is apt; it fulfills a certain number of functions to the cell, hence justification of its presence. It is further assumed that the similarities that exist in membrane composition and structure are due to the similarity of roles.

This ~~xxxxxx~~ approach of reconciling structure in terms of function on the cellular level is incomplete. In recent years it has been suggested that ~~x~~ a number of subcellular organelles in eucaryotic cells *particularly* (the mitochondrion and the chloroplast⁴⁴) *and the chloroplast* owe their origin to a primitive symbiosis, the organelle having previously been a bacteria. Thus, although much of the mechanism ^{now} of the organelle is ~~xxxxxxx~~ under central control, its very origin ^{perhaps} was not a response to evolutionary needs as much as the evolutionary manipulation of a coincidence.

log.c
A similar argument can now be applied to biological membranes. Arguments have been provided which indicate that the membrane may have preceded the cell. While it is evident that the membrane has evolved with the development of the cell, it may be just as correct to postulate that the cell also evolved to adapt to the properties of the membrane. In other words, since the glove came before the hand, the hand had first to fit the glove.

A number of cell characteristics can now be examined in terms of membrane properties rather than cell needs. It can be argued, for example, that the osmotic sensitivity of lipid-protein membranes forced cells which live under different tonic conditions (such as bacteria and plants) to develop cell walls, at considerable energetic and substrate expense. It can be maintained that the high water concentration in most cells (~~up to 90% in bacteria~~) is due to the membrane's free permeability to water.

TUSA

Even organisms which live outside of water require a high water concentration because their metabolism originated in dilute aqueous solution. In order to maintain the status quo, a high water level must be maintained.

Bacteria, for example, may contain up to 90% water (by weight). Why this great preponderance of water? Water, it can be argued, is the universal solvent. Organic chemists know that reactions in solvent occur much faster than mixing of two reactive powders. On the other hand, why should rate be a crucial in biological development? If the development of life itself took over a billion years, what difference should the rate of metabolism have on the organization of a particular organism. However, it could be that during the development of primitive cells, assuming the membrane hypothesis, these vesicles had no control over the water level. ~~Although~~ While the semi-permeable lipid and lipid-protein membranes are not ordinarily permeable to most chemical species, (itself constituting an advantage, ~~making~~ preventing high concentrations of necessary metabolites from diffusing out of the cell), they are freely permeable to water. ⁴⁵ These first organisms, then were prey to osmotic and chemical potential. The ~~water~~ intracellular water concentration was determined by the Donnan ⁴⁶ equilibrium. These cells may have had no alternative but to build their structure and metabolism in dilute aqueous medium, and thus it has remained. This high water level must still be maintained today in organisms which live outside the observation of water. Thus, ~~xxxxx~~ that cells require a high concentration of water in order for normal metabolism, may be due in part to historical necessity and subsequent adaptation, rather than an evolutionary search for the optimal water concentration.

Did you heard about "Pan-Sperima" hypothesis
of Krick?

CONCLUSION

-13-

The theories on the morphological development of primitive cells in the primeval sea divide into two categories: those in which a membrane composed of amphipathic molecules takes part, and those in which it does not. Since such membranes are so vital a part of biological machinery, it is difficult to believe that they were adsorbed onto an already metabolizing and reproducing cell. The fact that some membranes may be supplemented with extraneous lipids, and the inability of cells to synthesize membranes "de novo" ~~xxxxxxxxxxxxxxxxxxxx~~ indicates that a certain gulf exists between the membrane and the genes. These points support the theory that the morpho-^{was}logical basis of the cell lies in ~~the~~ aqueous membrane-bound vesicles ~~with~~ with the same general structure as present-day cell membranes, but perhaps of different composition.

The plausibility of this theory has the following corollary: when an attempt is made to explain the ubiquity of the biological membrane, both ^{the} metabolic function and the possible evolutionary significance should be considered.

It will be better to divide the last half of the seminar into headlines.

If you like to, it will be nice to add the aspect of "Vectorial metabolism" performed by the membrane.

Also, other two function of the membrane,

of the living cell: a) Non-polar environment. b) Organization of catalytic reaction ^(or more) that should be sequential. I wonder if one of these three functions should be considered as a vital functions for the primitive cell.

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of the final form,
for me

EXCELLENT

23. "Basic to the definition of a cell is a membrane separating the activities within it from the surrounding environment.

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for another
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